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Studies In Qualitative Organic Analysis.



**STUDIES IN QUALITATIVE ORGANIC
ANALYSIS**

BY

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THIS IS TO CERTIFY THAT THE THESIS PREPARED UNDER MY SUPERVISION BY

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ENTITLED STUDIES IN QUALITATIVE ORGANIC ANALYSIS

IS APPROVED BY ME AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE

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STUDIES IN QUALITATIVE ORGANIC ANALYSIS

PART I. THE FERRIC CHLORIDE HOMOLOGOUS TEST FOR PHENOLS

PART II. THE PREPARATION AND CHARACTERIZATION OF M-AMINO
ETHYL BENZENE

INTRODUCTION

When a new and unknown organic compound is prepared and isolated, the steps in its characterization are (1) purification, (2) qualitative analysis for the elements, (3) quantitative analysis, (4) molecular weight determination, and (5) determination of its atomic linking structure. The time required to perform the manipulation involved in the first four steps is at least four or five days, while the last step may require months. Obviously this method of procedure is not a desirable one for qualitative organic analysis due to the expense of time and materials, although it will always remain the last resort of the chemist when simpler and quicker methods fail.

A method of qualitative organic analysis, to be feasible, must require but a few hours to identify a given compound. Thanks to the untiring efforts of organic chemists,

enough common organic compounds and their derivatives have been characterized by the above laborious method to permit the use of a more feasible qualitative organic analysis based on different principles from the old method.

The modern methods of organic qualitative analyses are, as pointed out by S. P. Mulliken¹ in his admirable book, based on a determination of known characteristic physical and chemical properties of the substance examined. This method is just as certain in results and much simpler in operation than the old cumbersome and tedious method referred to above.

The scheme of analysis universally accepted to-day as being simplest and most exact is as follows:- The substance is (1) examined for its physical properties; (2) a qualitative analysis is made for the elements in the organic and inorganic form; (3) solubility reactions are studied; (4) tests are made for the homologous group to which the substance belongs; and (5) a simple derivative is made as a confirmation test. This thesis deals with a study of the latter two divisions as they are applied to phenols and aromatic amines.

It is fortunate indeed for the organic chemist that nearly every homologous series has a characteristic reaction peculiar to itself, as otherwise his task of analysis would be stupendous. Nearly every phenol will give a coloration with ferric chloride solution, and it has been this coloremtric reaction that has been one of the homologous tests for phenols and tautomers having the linkage $\text{H} - \underset{|}{\text{C}} = \underset{|}{\text{C}} - \text{O} - \text{H}$.

While this ferric chloride reaction has been used extensively in organic analysis as a general test for phenols, no attempt has ever been made to make this test more specific and by it to identify and confirm individual phenols; and to differentiate between them. The purpose of the first part of this investigation is an endeavor to devise a simple and systematic series of tests whereby it may be possible to differentiate the individual phenols definitely, one from the other, by the ferric chloride color reaction. The methods and tests used are those which suggested themselves as affording a natural and logical classification of the phenols into sub-homologous groups by the variation in color which they give with ferric chloride solution under varying conditions.

The second part of this investigation deals with the preparation and characterization of m-amino ethyl benzene and its acetyl and sulphonyl derivatives; the desire being to obtain these substances by standard methods^{of} synthesis which will give compounds of definite purity.

PART I

THE FERRIC CHLORIDE HOMOLOGOUS TEST

FOR PHENOLS

Historical

The fact that some organic compounds give a colored solution when treated with iron salts was known many hundred years ago. The preparation of writing fluids in the middle ages was based on this phenomena. The extract of gallnuts, which contains gallic acid, a derivative of trihydroxy phenol was treated with an iron salt whereupon a dark blue-black solution was obtained which made an excellent ink.

In 1834 Runge² discovered in the oil of coal tar at least six new compounds among which was phenol. Runge investigated the physical and chemical properties of these new substances and discovered that phenol gave a violet blue coloration with ferric chloride. He found that this coloration would not take place if alkalies, acids or alcohol were present. This phenomena is not peculiar to hydroxy benzene alone, since he found that any substituted phenol would give it.

This, therefore, is a class reaction, and it is remarkable that it was several years before any study was made of its mechanism. However, the hypothesis was made that the ferric chloride oxidized the phenyl radicle, and that several of the molecules then combined to form a colored complex.

The first systematic attempt at a study of this interesting reaction was made in 1871 by Hugo Schiff³. His observations led him to believe that the color obtained by treating a phenol with an iron salt was due to the presence of the hydroxyl group in the compound.

O. Hesse⁴ in 1876 endeavored to use the results of Schiff in determining the structure of a substance which he had prepared, and which he suspected to be a phenol. He discovered the fact that ferric chloride gave different colorations with the same phenol when different solvents were used. He observed that an aqueous solution of phenol gave a violet color with ferric chloride while an alcoholic solution of phenol gave no color at all. Upon adding alcohol to the aqueous solution of phenol he found that the violet color disappeared. A great deal of confusion resulted at this time by the fact that different investigators making the ferric chloride test on identical substances obtained varying results due to the use of different solvents.

W. Wislicenus⁵ in 1895 while investigating the tautomers of formal-phenyl acetic ester, tried the ferric chloride reaction of his compound, and found that the enolic form gave a coloration. He concluded that this coloration was a test for the $\text{H} - \text{O} - \underset{\text{|}}{\text{C}} = \underset{\text{|}}{\text{C}} -$ group. However, since he was not clear concerning the theory of this reaction, he did not attach much importance to it. He observed nevertheless that a distinction could be made between phenols and B-ketoesters. The former shows the color with iron best in aqueous solution,

and upon the addition of alcohol the color disappears, while the latter shows the color only when dissolved in alcohol.

However, Claisen⁶ was the first investigator to satisfactorily explain the mechanism of this reaction and to ascribe formulae to the colored organic iron salts formed.

Morrell and Crofts⁷ two Englishmen, prepared and isolated some of the iron organic compounds, among which were ferri-acetyl acetone $\text{Fe}(\text{C}_5\text{H}_8\text{O}_2)_3$ and ferri-benzoyl acetone, $\text{Fe}(\text{C}_{10}\text{H}_{10}\text{O}_2)_3$.

In 1902 Hantzsch and Desch⁸ published a paper, "Concerning Colored Organic Ferric Compounds". The authors took cognizance of the work done before them, and went into a thorough discussion of the theory of the reaction. They did a great deal of original investigation and succeeded in preparing a great number of the colored organic iron compounds. They made quantitative analysis of these substances, and studied their physical and chemical properties in detail.

From then on this subject has been an interesting field of investigation for chemists, and papers on the subject have followed each other in rapid succession. F. Raschig-Ludwigshafer² published in 1907 a paper, "The Iron Chloride Reaction of Phenols" in which he substantiates the theory of Claisen that the iron atom is attached to the oxygen atom in the phenol. This paper was delivered in 1900 before the Chemical Society of Heidelberg, but was received with so much skepticism that it was not until other investigators obtained similar results that the author published his own paper.

Kurt H. Meyer⁹ in 1911 worked on this subject and proved by means of conductivity data that hydrochloric acid was liberated in the solution of the phenol when ferric chloride was added.

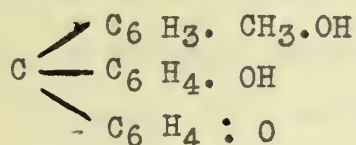
Knorr and Shubert¹⁰ worked out a method whereby they could tell exactly the percentage of enol and keto form of a substance that was present as a tautomer.

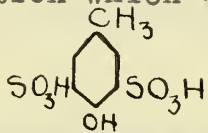
The latest work on the subject has been done by Weinland and Binder¹¹, in which they investigate the mechanism of, and products produced in, the reaction of ferric chloride on pyrocatechol and alizarin. Weinland and Herz¹² a year later made a study of the action of ferric chloride on salicylic acid.

However, it is surprising to find that none of these investigators made any attempt to use this characteristic reaction as a qualitative test for the detection of individual phenols.

Theoretical

The first theory concerning this ferric-chloride reaction was a hypothesis made by early chemists, before the reaction was really studied. It was thought that the ferric chloride oxidized the phenyl radicle in the para and ortho position, and that then several of the molecules combined to form a colored complex similar in nature to rosolic acid whose structure is



F. Raschig-Ludwigshafer² obtained a substance which contained radicles in the para and ortho position which were not liable to oxidation. This substance was  and showed with ferric chloride the characteristic color reaction thus disproving the above hypothesis.

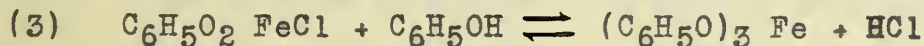
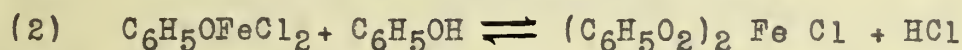
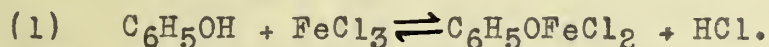
Schiff³ in 1871 concluded from the following experiments that the color was due to the presence of the hydroxyl group in the compound. He found (1) that all substances of the phenol type gave the color, (2) that the color did not appear when the hydrogen of the hydroxyl group was replaced by another radicle; and (3) that the intensity of the color depended upon the number of hydroxyl groups present in the substance.

Claisen⁶ in 1894 showed that the color formed by the action of ferric chloride on these weak organic acids was due to the actual formation of iron salts, and not to the oxidation of the compounds. Such salts were actually isolated and analyzed

among which were ferri-acetyl acetone, $\text{Fe}(\text{C}_5\text{H}_7\text{O}_2)_3$, ferri acetyl benzoyl acetone $\text{Fe}(\text{C}_{10}\text{H}_9\text{O}_2)_3$, and ferri di-benzoyl acetone $\text{Fe}(\text{C}_{17}\text{H}_{13}\text{O}_3)_3 \cdot 3\text{H}_2\text{O}$. Aluminum salts were also used and gave compounds of a nature similar to the iron salts.

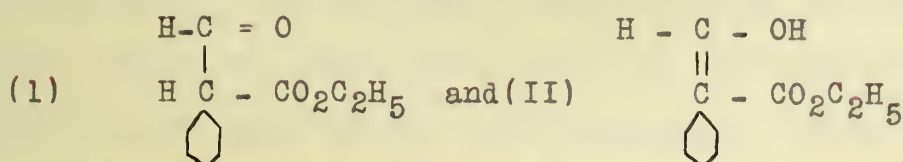
These organic salts of aluminium and iron possessed properties entirely different from true inorganic salts. They were not, at all, or only very slightly soluble in water, but dissolved readily in organic solvents such as alcohol, ether, chloroform, and benzene. They melted without decomposition and a few even boiled without breaking down so that their molecular weight could be determined and the above formulas substantiated. Their chemical properties were also different from the inorganic iron salts.

Claisen explained the mechanism of the reaction as follows:

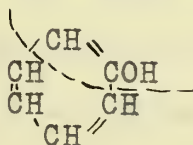


Claisen's work and conclusions have been substantiated and verified by other investigators working on the same problem and his theory is the one that is held to-day. This reaction produces hydrochloric acid which is a strong acid, by the displacement reaction of weakly acidic phenols according to the well-known partition principle of an insufficient amount of base between two acids.

Wislicenus⁵ in 1895 while working with formal-phenyl acetic ester which has the following tautomers



made the ferric chloride test and found that the second tautomer gave a color with ferric chloride. The only difference in these two tautomers is that (I) has the group $\text{H}-\underset{\text{O}}{\overset{|}{\text{C}}}-\underset{\text{H}}{\overset{|}{\text{C}}}-$ and that (II) has the group $\text{HO}-\underset{\text{H}}{\overset{|}{\text{C}}}=\underset{\text{H}}{\overset{|}{\text{C}}}-$ present. Therefore, the coloration must be due to the presence of the $\underset{\text{H}}{\overset{|}{\text{HOC}}}=\underset{\text{H}}{\overset{|}{\text{C}}}-$ group. This group is also contained in phenols as can be seen from the following structural formula of phenol



The part of the molecule in the dotted line being the familiar $\underset{\text{H}}{\overset{|}{\text{HOC}}}=\underset{\text{H}}{\overset{|}{\text{C}}}-$ group.

Wislicenus a year later attempted with fair success to use the color reaction to determine the equilibrium of the keto and enol forms of some tautomers. Using the same quantity of ferric chloride in each case, he found that the intensity of the color is proportional to the concentration of the enol form. Kurt H. Meyer⁹ determined the amount of enolate present by conductivity data. The reaction of the ferric chloride on the phenol liberates free hydrochloric acid, and the amount of the hydrochloric acid formed, as determined by the increased conductivity of the solution, is proportional to the amount of enol present.

Wislicenus showed that the iron compounds formed by the addition of ferric chloride to phenols are of the type FeR_2Cl and FeRCl_2 and not FeR_3 (R representing the organic radicle), since the latter does not give as intense a color, and is not as soluble as the first two salts. These three compounds possess different colors, and when small quantities of ferric chloride solution are added successively to formal-phenyl acetic ester (a compound which he was studying), the color change goes from red to violet-red, then to violet, then to blue-violet, and finally to blue.

The compound of the type FeR_3 does not conduct electricity in water solution and does not give a red color with KSCN , thus showing that it does not dissociate to give ferric ions. Knorr and Shubert¹⁰ found that the maximum of color intensity is in all cases given by the addition of two moles of ferric chloride to one mole of FeR_3 according to the following reaction, $\text{FeR}_3 + 2\text{FeCl}_3 \rightleftharpoons 3\text{FeCl}_2\text{R}$.

These ferric organic salts are decomposed by strong alkalies, but only slowly by ammonia. However, some compounds like salicylic acid or pyrocatechol give a color that is not destroyed even by alkalies. With hydrochloric acid these salts suffer decomposition which takes place in steps with the formation of intermediate compounds of the form FeR_2Cl , and FeRCl_2 .

Hantzsch and Desch⁸ compiled a list of the homologues that give the ferric chloride color test. These are (1) mono- and poly-phenols and their derivatives, (2) aromatic amino-phenols, especially those containing several amino groups,

(3) Enols, (4) Derivatives of malonic ester with negative substitutes in the methylene group, (5) many (not all) isonitro compounds e.g. phenyl isonitromethane, (6) numerous hydroxyl amine derivatives as Oximes, (8) certain compounds containing sulphur, as HSCN, and others. Exceptions to above classifications are known.

A compound of especial interest which they studied is salicylic acid. They isolated the ferric compound of this phenol and determined its physical and chemical properties. The color that ferric chloride gives with salicylic acid is due to the substitution of the hydrogen of the hydroxyl and not of the carboxyl group and its structure corresponds to the formula

(I) $(\text{C}_6\text{H}_4 \begin{smallmatrix} \text{O} \\ \diagdown \\ \text{CO}_2\text{H} \end{smallmatrix})_3 \text{Fe}$ and not to (II) $(\text{C}_6\text{H}_4 \begin{smallmatrix} \text{OH} \\ \diagdown \\ \text{CO}_2 \end{smallmatrix})_3 \text{Fe}$. They proved this by a pretty experiment in which they prepared first the ether $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{OCH}_3 \\ \diagdown \\ \text{CO}_2\text{H} \end{smallmatrix}$, which did not give the color with ferric chloride, and, second, the ester $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{OH} \\ \diagdown \\ \text{CO}_2\text{CH}_3 \end{smallmatrix}$, which did thus showing that the hydroxyl group was the one that took part in the reaction.

The fact that the addition of alkali does not destroy the ferric chloride color of salicylic acid is due to the reaction of the alkali with the carboxyl group. But an excess of alkali will remove the color.

There are three methods for the preparation of these organic iron salts, (1) by the addition of an aqueous solution of ferric chloride to an alcoholic solution of the organic compound to which sodium acetate has been added. The salt precipitates out or can be dissolved out by shaking with ether and then

subsequent evaporation of the ether. (2) When the iron salt is very soluble in H_2O and cannot be extracted with ether it can be prepared as follows:- Treat ferric ethylate $(C_2H_5O)_3Fe$ with the phenol, and the following reaction takes place

$(C_2H_5O)_3Fe + 3HR \rightleftharpoons FeR_3 + 3C_2H_5OH$, the only by-product being alcohol which can be evaporated off. There is no hydrochloric acid formed in this reaction and this method of preparation must be used whenever the salt formed is attacked by dilute acid.

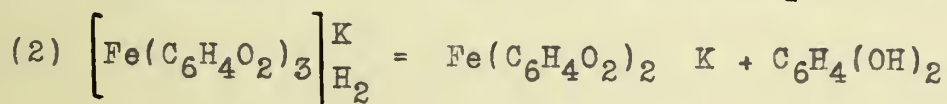
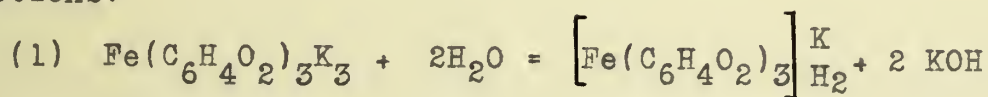
(3) The action of the phenol on colloidal ferric hydroxide will give the ferric salt. However, most of the phenols are very weak acids and this reaction may not take place readily.

The behavior of pyrocatechol with iron salts is very peculiar. Weinland and Binder¹¹ found that when iron chloride is added to an aqueous solution of pyrocatechol, a green color is obtained which upon the addition of alkalies changes to a dark red. They prepared the iron salt as follows:- A concentrated solution of pyrocatechol is added to a strong solution of potassium hydroxide and this is treated with a concentrated solution of ferri-acetate whereupon a precipitate settles which is the iron organic salt in an impure state. This compound is readily soluble in water but when acid is added the color disappears. Its composition corresponds to the formula $(\text{C}_6\text{H}_4\text{O}_2)_3Fe$. The iron is firmly held by the organic radicle even when the solution is alkaline and it can be boiled a long time without the alkali precipitating the iron.

The change in color from green to red on the addition of alkali is explained as follows:- In the green solution the iron

is bivalent while in the red solution it is trivalent. In alkaline solution pyrocatechol is oxidized by the air which in turn oxidizes the iron to the trivalent form, while in the neutral and acid solution the iron is reduced by the pyrocatechol.

When the experiment is conducted in an atmosphere of hydrogen with the exclusion of air, only a very pale red coloration takes place upon the addition of potassium hydroxide to the green solution. If now the solution is exposed to the air a deep red color is formed. This red colored solution, on extreme dilution with water becomes red violet and then suddenly violet, due to hydrolysis. The red color is due to $\text{Fe}(\text{C}_6\text{H}_4\text{O}_2)_3\text{K}_3$ and the violet color is due to the formation of $\text{Fe}(\text{C}_6\text{H}_4\text{O}_2)_2\text{H}$. The color change which takes place with hydrolysis is due to the following reactions:



These violet salts were isolated and found to be insoluble in alcohol. With the addition of mineral acids their color is destroyed because the complex ferric compound decomposes. Alkalies dissolve the violet salt and form a deep red colored trivalent iron compound.

The theory of the ferric chloride reaction has been investigated extensively and a great number of the ferric organic compounds have been isolated. These different iron salts are varicolored depending on the organic radicle in the compound and

it seems very probable that a method of differentiation between the phenols could be evolved by the ferric chloride color reaction.

Experimental

Introduction

The purpose of the following experiments is to make a series of tests on different phenols and, if possible, to identify the different phenols by their different behavior. It seems only natural that different phenols should give different colorations with ferric chloride solution and the probability is that every phenol does give a different colored iron salt. However, in some cases the difference in color and shade is so slight that it is not perceptible to the eye.

Some of the colors given by phenols are very delicate and often^{of} a transitory nature, while others are very stable and remain indefinitely. Some phenols give a color with a certain concentration of ferric chloride which may disappear upon the addition of more of the reagent, while others show no color until a large excess of ferric chloride is added. Again, the solvent used has a marked influence on the character and intensity of the color. Some phenols give a color in aqueous but not in alcoholic solution while others give the color under reversed conditions; and still others show a coloration in both solutions. Obviously when dealing with compounds of such a sensitive and varying nature it is essential that all the factors of the experiment be known, and that every factor but the one being studied should be kept constant in order that only known variables are operative.

Preparation of Solutions

Two separate ten per cent ferric chloride solutions were prepared; one of water, the other of absolute alcohol. The latter solution being used with solutions of phenols in absolute alcohol, thus excluding all water from the solution. It is interesting to note that a true salt like ferric chloride dissolves readily in pure alcohol.

The hydrochloric acid and potassium hydroxide solutions used in the tests were also ten per cent solutions.

Three separate solutions of one per cent strength were made of each phenol in the following solvents: (1) water, (2) 95% alcohol and (3) absolute alcohol. Some phenols failed to dissolve completely in one or more of these solvents but the tests were made on these solutions anyway.

Effect of Solvent on Color

Five cubic centimeters each of the aqueous, 95% alcohol, and absolute alcohol solutions of the same phenol were taken in three separate test tubes. To the absolute alcohol solution a drop of absolute alcoholic ferric chloride solution was added, while to the aqueous and 95% alcoholic solution, a drop of aqueous ferric chloride solution was added; the color change, if any, being noted in each instance. In order to study the effect of dilution, the alcoholic solutions were treated with water, and the water solution was treated with alcohol; any color changes being observed. A blank test was made by adding a drop of ferric chloride solution to pure water, 95% alcohol, and absolute alcohol. The water is scarcely colored, but the alcohol is

colored a citron yellow which often blends with, or masks entirely the delicate color given by some phenols. The results obtained are given in Table I, following.

Effect of Acid and Alkali on Color

To the water and alcohol solutions of each phenol, to which a drop of ferric chloride solution was added, hydrochloric acid is added drop by drop until a large excess is present; note being made of any color changes. The same procedure is gone through with using potassium hydroxide instead of hydrochloric acid. The results are shown in Table II, following.

Effect of Concentration

With a change in concentration of solutions and reagents different results are obtained. A dilute solution of phenol in alcohol gives no color with ferric chloride and upon the addition of water the solution still remains colorless. A concentrated solution of phenol in alcohol also gives no color with ferric chloride but now upon the addition of water the characteristic violet color appears.

When adding potassium hydroxide to salicylic acid, a red color is formed upon the addition of one drop, which disappears on adding more of the reagent. Again when the red solution obtained by adding a drop of ferric chloride to alkaline pyrocatechol is diluted a violet color is formed due to hydrolysis.

Hence it is seen that the ferric chloride reaction with phenols is a sensitive and peculiar one and it is only by careful control that comparable results can be obtained.

TABLE I
INFLUENCE OF SOLVENTS

Substance	Color in aq. sol.	Color in 95% alc. sol.	Color in abs. alc. sol.	When alcohol is added to aq. sol.	When water is added to alc. sol.
Phenol	violet	- -	- -	color disappears	- -
Pyrocatechol	deep green	deep green	deep green	- -	- -
Resorcinol	deep violet	- -	- -	disappears	- -
Hydroquinone	green (changes to brown)	- -	- -	- -	- -
Pyrogallol	brown	deep green	deep blue	- -	faint green
Phloroglucinol	violet	- -	- -	disappears	- -
O-Cresol	deep blue (turns turbid green)	- -	- -	disappears	- -
M-Cresol	violet	- -	- -	disappears	- -
p-Cresol	deep blue	- -	- -	disappears	- -
o-nitro Phenol	- -	brown	light brown	- -	disappears
p-Nitro Phenol	wine red	brown	- -	disappears	- -
Salicylic acid	deep violet	deep violet	deep violet	- -	- -
α -naphthol	white ppt.	- -	- -	ppt dissolves	- -
β -naphthol	- -	- -	- -	- -	- -
Resorcin	violet	- -	- -	disappears	- -
Thymol	- -	- -	- -	- -	- -

N.B.- A dash indicates that no color change took place

Substance	Effect of KOH solution	Effect of HCl solution
Pyrocatechol	deep red; clear solution	color disappears
Salicylic acid	deep red (disappears with excess)	" "
α -naphthol	green precipitate	" "
Pyrogallol	deep purple turbid solution	" "
Phenol	Color disappears; ppt of $\text{Fe}(\text{OH})_3$ formed	" "
Resorcinol	"	" "
Hydroquinone	"	" "
o-nitro Phenol	"	" "
p-nitro phenol	"	" "
o-Cresol	"	" "
m-Cresol	"	" "
B-naphthol	"	" "
phloroglucinol	"	" "
orcin	"	" "

SUB-HOMOLOGOUS GROUPS

Color given in aqueous solution	Color given in alcoholic solution	Color given in aqueous and alcoholic solution
Phenol	O-nitro Phenol	Pyrocatechol
Resorcinol	Pyrogallol	Salicylic Acid
Hydroquinone		
Phloroglucinol		
o-Cresol		
m-Cresol		
p-Cresol		
p-nitro Phenol		
orcin		

Thymol and B-naphthol do not give any coloration with ferric chloride at the concentrations on which this experiment was carried out and α -naphthol gives a white precipitate with ferric chloride but no coloration.

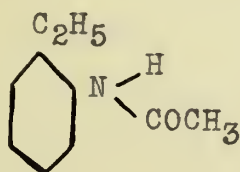
Conclusion

From the above experiments it is seen (1) that most phenols give a color with ferric chloride in aqueous solution; (2) that the colored solution disappears in all cases upon the addition of hydrochloric acid; and (3) that the addition of potassium hydroxide destroys the color and forms a precipitate of ferric hydroxide, with the exception of the four cases given in table II. A classification of phenols into three sub-homologous groups is shown in table III according to whether the color with ferric chloride is given in aqueous solution, alcoholic solution, or both. The phenols within these sub-homologous groups may be distinguished from each other by the different colored solutions which they give with ferric chloride and by their subsequent behavior when treated with potassium hydroxide. Many phenols show such a characteristic behavior in these reactions that they can be recognized immediately in qualitative organic analysis without recourse to the customary confirmatory test.

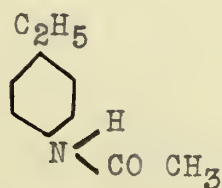
PART II
PREPARATION AND CHARACTERIZATION OF M-AMINO ETHYL
BENZENE

Historical

The only record of the preparation and characterization of m -amino ethyl benzene found in the literature is a brief account by Behal and Choay¹, two Frenchmen, published in 1894. The compound was prepared as follows:- Ethyl benzene was nitrated with fuming nitric acid; ortho and para nitro ethyl benzene being formed according to the well-known theory of orientation; 66% of the yield being ortho and 34% para. This mixture of ortho and para nitro-derivatives was then reduced to the corresponding amines by treatment with iron and acetic acid. The mixture of amines obtained was then treated with acetic anhydride thus giving the ortho and para acetyl derivatives corresponding to the following formulae:



ortho



para

These acetyl derivatives were separated by crystallization. The para derivative was now nitrated with a calculated amount of fuming nitric acid; the nitro group going into the ring meta to the ethyl radicle and ortho to the substituted

amine radicle, according to the rules of orientation. The following substance being obtained,

(1) $\text{C}_2\text{H}_5 \cdot \text{C}_6\text{H}_3 \begin{matrix} \nearrow \text{NO}_2(3) \\ \searrow \text{NH.CO.CH}_3(4) \end{matrix}$ which is then converted back to an amine by saponification with hydrochloric acid and then subsequent treatment with sodium hydroxide. The amine group is then removed by the familiar diazo reaction, the final product being meta nitro ethyl benzene which was then reduced to the corresponding amine. This substance is a liquid at ordinary temperature; boils at 214-15°C; and its specific gravity is 0.9896 at 0°. Its acetyl derivative melts at 24-25° and boils at 312-13°C. without decomposition. This method of preparation is cumbersome and involved and yields only 12% of the initial product used.

Theoretical

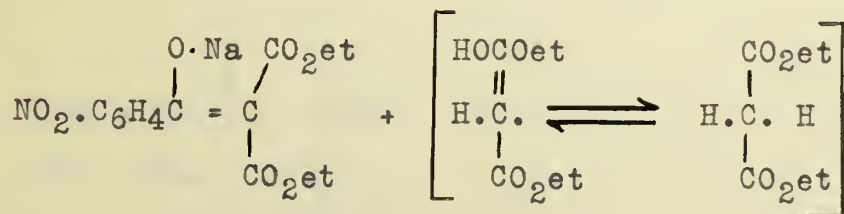
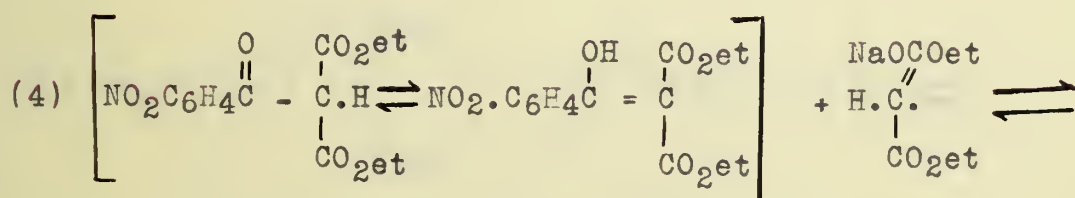
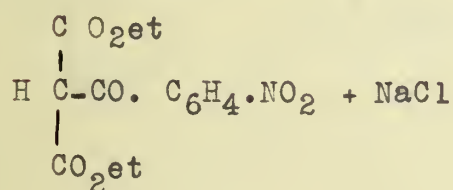
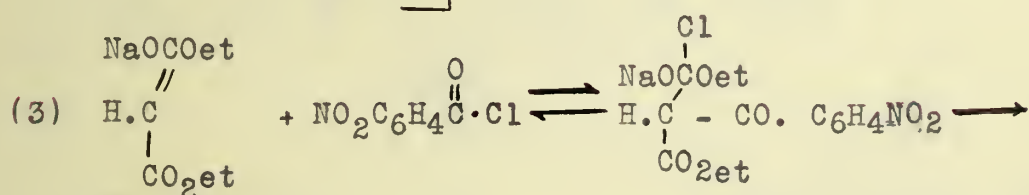
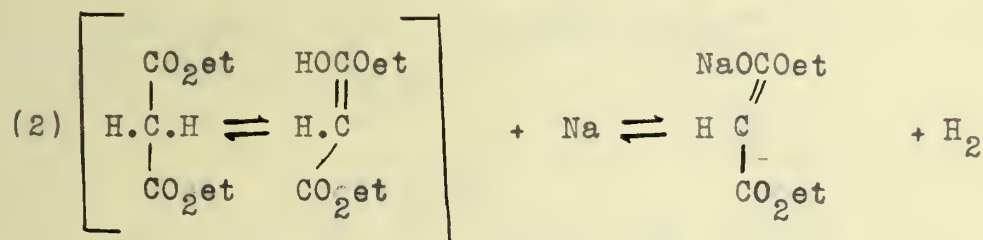
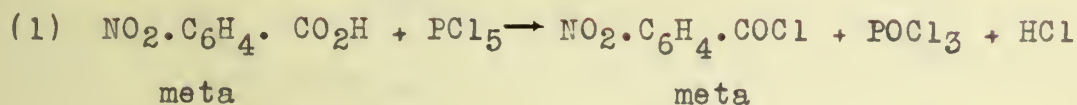
It is questionable whether m-amino ethyl benzene prepared by the method of Behal and Choay can be thoroughly separated from its isomers and purified. Furthermore, this method is too long and cumbersome, and gives a very poor yield. Therefore, a simpler synthesis has been evolved which will give better yields of the product in a pure state.

To study the preparation of a compound in a scientific manner it is necessary to first predict the collisions that result in chemical reactions under the conditions of the experiment; and from a knowledge of the relative velocities of these reactions to predict the best mass relationship and temperature of experimentation. Further, in the case of equilibrium reactions the conditions which will drive the reaction to completion must be determined. This last factor necessitates a thorough knowledge of the physical properties of the substances used and formed in the experiment.

The method chosen for the preparation of m-amino ethyl benzene in the pure condition is the condensation of m-nitro-benzoyl chloride with the sodium enolate of malonic diethyl ester, with the subsequent production of m-nitro-benzoyl acetic acid. This product by means of the ketone decomposition is converted into m-nitro phenyl methyl ketone (m-nitro acetophenone). This product is now reduced by steps into the desired m-amino ethyl benzene.

✓ The collisions resulting in chemical reactions under

the conditions of this synthesis of m-nitro benzoyl malonic diethyl ester are as follows:



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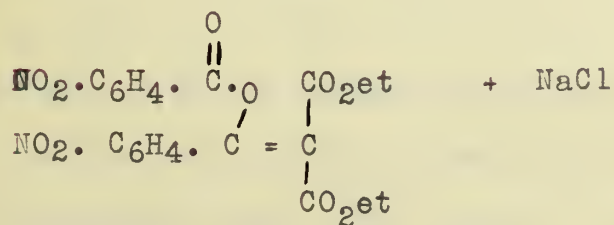
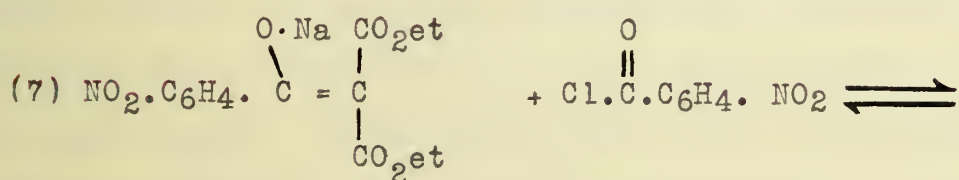
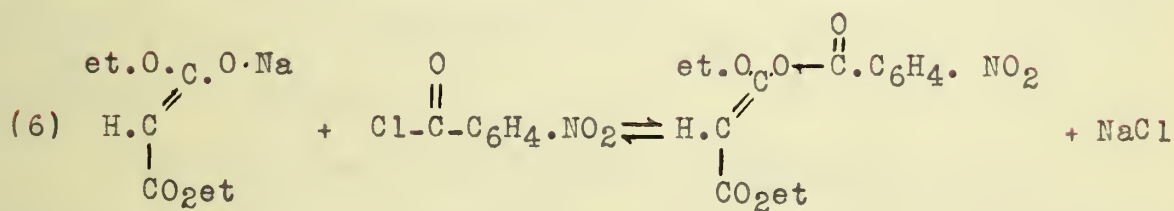
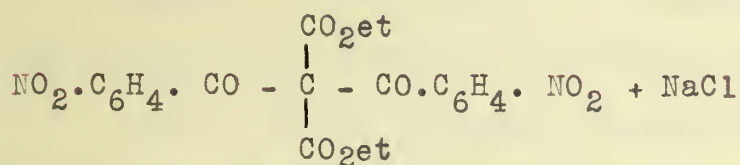
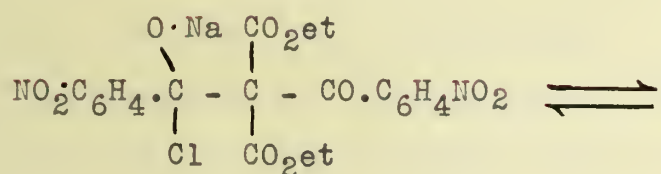
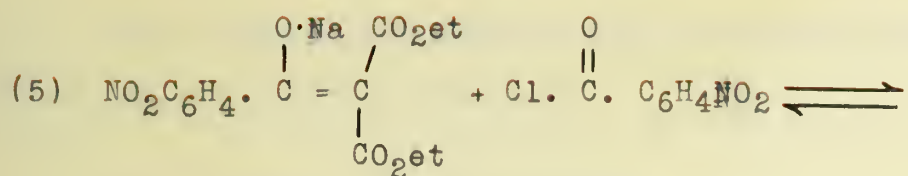
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The relative velocities of the reactions can only be stated qualitatively as follows:

- A. Reaction (1) very rapid
- B. Reaction (2) is very rapid
- C. Reaction (3) is much slower than (2)
- D. Reaction (4) is rapid like (2)
- E. Reaction (5) is similar in velocity to (3)
- F. Reactions (6) and (7) are slower than reactions (3) or (5) and are therefore the slowest reactions.

Obviously reactions (2) and (3) are those desired, but reactions (3) and (4) will be appreciable and cannot be avoided from the standpoint of velocity.

The influence of the relative proportions of the initial materials (mass action) upon the course of the reaction must next be studied. An excess of the sodium enolate of malonic ester over the acyl chloride would favor the desired reaction (3); an excess of the free malonic ester would give the same results. Unfortunately the study of the physical properties show that very little sodium enolate of malonic ester is soluble in ether; and alcoholic solvents cannot be used because of their reaction with the acyl halide. Hence it is seen that the solubilities of the compounds favor a mass relationship which will produce di-alkyl malonic di ethyl ester formation. However, the reactions were carried out using molar proportions and the results are discussed in the experimental part.

The further steps for the production of the m-amino

ethyl benzene were not carried out due to insufficient time, so no discussion of their theory will be given.

Experimental

Preparation of M-Nitro-benzoic Acid

As there was an insufficient supply of m-nitro-benzoic acid at hand, more was prepared by the nitration of benzoic acid. The preparation and purification taking place as outlined in the Laboratory Manual of W. A. Noyes². The melting point of the acid thus prepared was 141°C. (corrected) and the yield was 70%.

Preparation of M-Nitro-Benzoyl Chloride³

65 grs. of m-nitro-benzoic acid was mixed gradually with 85 grs. of powdered phosphorous penta-chloride. A little more than equal molar weight of the latter being used because of moisture in the acid and impurity of the phosphorous penta-chloride. Upon mixing these two solids a liquid was formed and hydrochloric acid gas was evolved. The phosphorous oxychloride formed was distilled off under diminished pressure. Then the temperature was raised and the excess phosphorous pentachloride was driven off. Finally the product was distilled at 185° (uncor.) under a pressure of 50-55 mm. A heavy light yellow oil was collected which on standing, solidified in long flat needles. These crystals melted at 31-35°. Yield was 48 grams, which corresponds to 66% of theory.

Preparation of M-Nitro-benzoyl Malonic Ester.

42 grams of freshly purified malonic ester was placed in a flask fitted with a reflux condenser and 150 cc. of absolute ether was added as a solvent. 5.83 grams of finely cut sodium was dropped gradually into the malonic ester whereupon hydrogen gas was evolved and a white soapy voluminous solid separated out, which was the sodium enolate of malonic diethyl ester. To this was now added an absolute ether solution of the 48 grams of m-nitro-benzoyl chloride, prepared in the experiment above. This mixture was refluxed for twenty-four hours on a hot plate, then water was added which dissolved out the sodium chloride formed. The ether solution formed a layer above the water and was separated and dried with anhydrous sodium sulphate. The water solution was saved and examined later. Upon evaporating the ether solution on a water bath a brown oily liquid was obtained. On standing over night in a cool room this liquid solidified as a crystalline mass interspersed with liquid. Slight warming melted or caused the crystals to dissolve again. This substance was tested for sodium in the flame and none was found present, thus showing it not to be a sodium salt. Upon adding a drop of ferric chloride to an alcoholic solution of the substance a deep wine colored solution was obtained showing the presence of a tautomer.

Purification

The yellow oil obtained above was put in a Claisen distilling flask and the excess of malonic ester was distilled off and collected. This malonic ester boiled at 199° (corrected)

The residue was poured from the flask into a beaker and cooled down with a freezing mixture, but only became more viscous and would not crystallize. Ether was added to this cold viscous mass and stirred vigorously whereupon some of it went into solution leaving a flocculent precipitate suspended. This solution was filtered and the precipitate purified by dissolving it in hot alcohol and then precipitating it by cooling. Upon filtering, a pure white fibrous substance was obtained, which was dried. This substance melted at 95° (corrected) and the yield was five grams. It did not show a coloration with ferric chloride showing it was not a tautomer.

The ethereal filtrate of above was evaporated down on a water bath and a viscous oil was again obtained, which was distilled under diminished pressure and more malonic ester driven off. The residue was completely dissolved in alcohol and cooled with the expectation of obtaining a precipitate similar to the previous one. A precipitate did come out but it was an oily substance and upon standing settled to the bottom. The clear alcohol solution was poured off and evaporated and a small amount of the above viscous oil obtained as a residue.

This oil was allowed to stand eleven days whereupon it formed a crystalline mass interspersed with liquid, which was then treated with cold ether. The interspersed liquid went into solution and the crystals remained behind. The solution was filtered and the crystals dissolved in hot alcohol and crystallized out, by cooling. They were collected on a filter and dried. This substance melted at 95° (corrected) and the yield

was eight grams. This substance also did not show a color with ferric chloride and when mixed with the solid obtained previously, and melted, did not change its melting point, thus showing it to be the same substance.

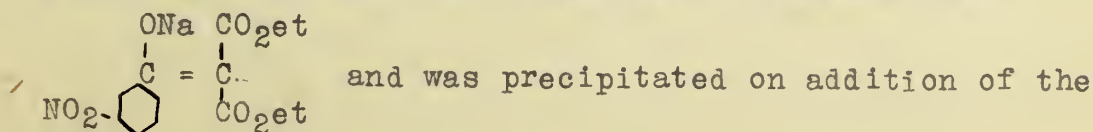
Analysis

The substance obtained above was analyzed for nitrogen by the combustion tube method. Two analyses were made using approximately .25 grams of substance in each case, and the following results obtained:

Results			
	N found in substance	N calculated in m-nitro-benzoyl malonic diethyl ester	N found in di-m-nitro benzoyl diethyl malonic ester
No. 1	5.98%	4.84%	6.11%
No. 2	6.45%		

This proves the substance to be the di-m-nitro benzoyl malonic ester and its inaction with ferric chloride confirms this.

The water solution obtained above which was separated from the ether solution was treated with dilute sulphuric acid whereupon a white flocculent precipitate was thrown down. This was purified by crystallizing from alcohol and dried; and a melting point determined. It melted at 108° (corrected) and gave a brown coloration with ferric chloride; yield was .5 gr. This substance must have been dissolved in the water as



sulphuric acid which displaced the equilibrium to the keto form.

Unfortunately sufficient time was not available to furnish the synthesis and to more definitely characterize these intermediate products.

Conclusion

(1). M-nitro benzoyl malonic ester cannot be prepared in appreciable amounts by the action of m-nitro benzoyl chloride on the sodium enolate of malonic diethyl ester in ether solution.

(2). Di-m-nitro benzoyl malonic ester has been prepared and characterized for the first time, by the action of m-nitro-benzoyl chloride on the sodium enolate of malonic diethyl ester in ether solution. It is a white crystalline solid which melts at 95° (corrected).

(3). A white crystalline product is formed simultaneously with the di-m-nitro benzoyl chloride and melts at 108° (corrected).

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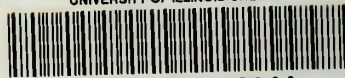
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